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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,872	02/21/2002	Walter Callen	564462006100	9897

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VERENIUM C/O MOFO S.D.
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
11/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/081,872	CALLEN ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007 and 28 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *74,108,112-116,118-121,147-166 and 176-239* is/are withdrawn from consideration.

5)☒ Claim(s) *2-4,47,105,122,124,131,143-146,240 and 241* is/are allowed.

6)☒ Claim(s) *1,6,14-17,48,75,76,88,89, 92,103,106,107,130,132-135,138-142 and 242* is/are rejected.

7)☒ Claim(s) *102 and 104* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 August 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-4,6,14-17,47,48,74-76,88,89,92,102-108,112-116,118-122,124,130-135,138-166 and 176-242.

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submissions filed on 8/08/07 and 8/28/07 have been entered.

Claims 5, 7-13, 18-46, 49-73, 77-87, 90-91, 93-101, 109-111, 117, 123, 125-129, 136, 137, and 167-175 have been canceled. Claims 1-4, 6, 14-17, 47, 48, 74-76, 88, 89, 92, 102-108, 112-116, 118-122, 124, 130-135, 138-166 and newly presented claims 176-242 are still at issue and are present for examination.

Claims 74, 108, 112-116, 118-121 and 147-166 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the response filed 6/23/03. Newly presented claims 176-239 recite methods which are patentably indistinct from the methods of withdrawn claims 147-166 which are patentably distinct from the elected invention

as explained in the office action of 9/25/06. As such claims 176-239 are withdrawn herein. Claims 1-4, 6, 14-17, 47, 48, 75-76, 88, 89, 92, 102-107, 122, 124, 130-135, 138-146 and newly presented claims 240-242 are examined herein.

Claims 102-104 are objected to because of the following informalities: "comprising a sequence as set forth in claim 2" should say "comprising a nucleic acid as set forth in claim 2". Appropriate correction is required.

Claims 14, 15, 17, 48, 132-135 and 138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 15, 48, 134, and 135 (upon which claims 132, 133 and 138 depend) are vague and indefinite in the recitation "at least about" as "at least" and "about" are inconsistent as "at least" requires a definite lower limit, while "about" does not.

Claim 17 is confusing in the recitation of "nucleic acid of a sequence claim 1 or claim 2". It is suggested that "a sequence be deleted". Furthermore, all of the recitation following the term "wherein" does not appear to add anything to the claim as the conditions recited in the claim are low stringency conditions. Any probe comprising a nucleic acid of claim 1 or claim 2 could hybridize to SEQ ID NO:125 under these

conditions. It is suggested that this entire portion of the claim be deleted.

Claim 48 is confusing in the recitation of "A method of producing a polypeptide having amylase activity, comprising the steps of: providing a nucleic acid having the nucleic acid sequence of claim 1" as the nucleic acids of claim 1 do not necessarily encode an amylase as the nucleic acids of claim 1 encompass the complements of nucleic acids encoding amylases as well. Furthermore it is noted that claim 1 does not recite a nucleic acid sequence but a nucleic acid such that the claim should recite providing a nucleic acid of claim 1.

Claims 75, 76, 88, 89, 92, and 242 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 75, 76, 88, 89, 92, and 242 are drawn to polynucleotides which hybridizes to the polynucleotide of SEQ ID NO:125 or the nucleic acid of claims 1 or 2 under low or high stringency conditions. The claims are directed to a genus of polynucleotides and variants and fragments thereof that have not been disclosed in the specification. No description has been

provided of the structure and function of the modified polynucleotide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:125 which encodes the amylase of SEQ ID NO:126 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polynucleotides. The specification does not contain any disclosure of the structure and function of all the polynucleotide sequences derived from SEQ ID NO:125, including fragments and variants within the scope of the claimed genera. The genera of polynucleotides claimed is a large variable genus including polynucleotides which can have a wide variety of structures and functions. The specification discloses only a small number of species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants appear to believe the amendments to the claims overcome the instant rejection. However, the rejected claims still include no functional limitation and are not limited to a genera of nucleic acids for which all members have a disclosed function. Therefore, the rejection is maintained for these claims.

Claims 1, 6, 16, 17, 48, 75, 76, 88, 89, 92, 130, 139-142 and 242 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding proteins having 95% identity to SEQ ID SEQ ID NO:126 and alpha amylase activity, does not reasonably provide enablement for any polynucleotide encoding a protein having 90% identity to SEQ ID NO:126 and alpha amylase activity or any polynucleotide having at least 90% sequence identity to SEQ ID NO:125 and encoding a polypeptide with an alpha amylase activity or any polynucleotide comprising a fragment of SEQ ID NO:125, or all fragments and variants thereof or vectors and host cells comprising said nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 6, 16, 17, 47, 48, 75, 76, 88, 89, 92, 122, 124, 130, 139-142 and 242 are directed to any polynucleotide encoding

a protein having 90% identity to SEQ ID NO:126 and alpha amylase activity or any polynucleotide having at least 90% sequence identity to SEQ ID NO:125 and encoding a polypeptide with an alpha amylase activity or any polynucleotide comprising a fragment of SEQ ID NO:125, or all fragments and variants thereof or vectors and host cells comprising said nucleic acids. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding amylases and variants and fragments thereof broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide of SEQ ID NO:125 which encodes the alpha amylase of SEQ ID NOS 126.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions

or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass an enormous number of polynucleotide fragments and variants of the polynucleotide of SEQ ID NO:125 because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting amylase activity; (B) the general tolerance of amylases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the

claimed invention in a manner reasonably correlated with the scope of the claims broadly including an enormous number of polynucleotide fragments and variants of the polynucleotide of SEQ ID NO:125. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants appear to believe the amendments to the claims overcome the instant rejection. However, the rejected claims still encompass a scope of nucleic acids for which the amount of experimentation which would be required to enable the full scope of the instant claims is undue for all the reasons presented herein and in the previous Office actions.

Claims 103, 106, 107 and 140 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell transformed with the synthetic nucleic acid, does not reasonably provide enablement for host cells within a multicellular organism that have been transformed with the synthetic nucleic acid. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 103, 106, 107 and 140 are so broad as to encompass host cells transformed with specific nucleic acids, including cells in *in vitro* culture as well as cells within any multicellular organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cells broadly encompassed by the claims. While methods for transforming cells *in vitro* are well known in the art, methods for successfully transforming cells within complex multicellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within one multicellular organism are unlikely to be applicable to transformation of other types of multicellular organisms as multicellular organisms vary widely. However, in this case the disclosure is limited to only host cells *in vitro*. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multicellular organism for the production of polypeptide. The

scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, expression of genes in a particular host cell and having the desired biological characteristics is unpredictable the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is suggested that applicants limit the claims to "An isolated host cell …".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 75, 76, 92 and 242 are rejected under 35 U.S.C. 102(b) as being anticipated by Tachibana et al. (Reference AK of applicant's IDS).

Tachibana et al. teach the isolation and expression of a polynucleotide encoding *Pyrococcus* sp. KOD1 alpha amylase. This polynucleotide has 80% identity to SEQ ID NO:125, encodes a protein with 85% identity to SEQ ID NO:126) and thus would hybridize to SEQ ID NO:125 under the low stringency conditions recited in these claims. The polynucleotide of Tachibana et al.

also comprises a region of 32 consecutive nucleotides with 100% identity to a region of SEQ ID NO:125 (i.e., nucleotide 1193-1224 of Tachibana et al. are identical to residues 748-779 of SEQ ID NO:125) which would hybridize to SEQ ID NO:125 under high stringency conditions.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 88 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tachibana et al. (Reference AK)

Tachibana et al. is discussed above. The nucleic acid of Tachibana et al. differs from those of the instant claims only in that the nucleic acids of the claims include a detectable label.

As the identification of other amylase genes would be desirable, it would have been obvious to one of ordinary skill in the art to label the nucleic acid of Tachibana et al. in order to use this nucleic acid as a probe for related amylase genes of other organisms. Use of any of the many well known types of labeling compounds (radioisotopes, fluorescent compounds, chemiluminescent compounds, enzymes such as horse radish peroxidase or alkaline phosphatase, etc. or haptens) would have been obvious to one of skill in the art.

Claims 2-4, 47, 105, 122, 124, 131, 143-146 and 240-241 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652